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TITLE: **Ketamine as a Rapid Treatment for Post-Traumatic Stress Disorder**

PRINCIPAL INVESTIGATOR: **Dennis Charney, MD**

CONTRACTING ORGANIZATION: **Mount Sinai School of Medicine**
New York, NY 10029-6574

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Dennis Charney, MD
Email: dennis.charney@mssm.edu

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Mount Sinai School of Medicine
New York, NY 10029-6574

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14. ABSTRACT

Post-traumatic stress disorder (PTSD) is a debilitating anxiety disorder characterized by intrusive re-experiencing of the traumatic events, avoidance of situations and stimuli that could serve as reminders of these events, and chronic hypervigilance. Patients with PTSD are often also depressed, and many have significant memory impairments. In the present study, we expect a single ketamine infusion to reduce core PTSD symptoms. In addition, in those patients with PTSD who are depressed, we expect ketamine to reduce depressed mood. Finally, ketamine is known to impair memory function. We will also test if the extent of ketamine-induced memory impairment during the infusion can predict how well people do after the infusion. The first patient was randomized at the end of May '09 as recruitment began in March '09. To date, seven people have been randomized of which have five have completed study procedures.

15. SUBJECT TERMS
Post-traumatic stress disorder, PTSD, ketamine, midazolam, depression, anxiety, memory

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Introduction

Post-traumatic stress disorder (PTSD) is a debilitating anxiety disorder characterized by intrusive re-experiences of the traumatic events, avoidance of situations and stimuli that could serve as reminders of these events, and feeling jumpy or easily startled. Patients with PTSD are often also depressed, and many have significant memory impairments. Existing drug treatments are unsuccessful in a majority of patients, especially in those with combat-related PTSD. The primary aim of the current study will test the efficacy of a single sub-anesthetic IV dose of ketamine in providing rapid relief of symptoms in patients with active PTSD. Ketamine-induced memory impairment will also be tested as a predictor of outcome. The effects of ketamine will be compared with that of the commonly used benzodiazepine anesthetic, midazolam, which is expected to mimic some of the acute dissociative effects of ketamine but not have any sustained anxiolytic and antidepressant effects. Forty individuals diagnosed with post-traumatic stress disorder, combat-related or civilian-related, will be included in this study.

Body

As per our Statement of Work (submitted 08/29/08), the following major tasks planned for months 1-12 are provided below in the left-hand column. Progress on these tasks is described in the right-hand column.

Major Task	Progress
Advertise study	Ongoing. We currently advertise the study on clinicalconnection.com, clinicaltrials.gov, craigslist, the Village Voice backpages and Biotrax
Recruit research participants	Ongoing. Twenty-six individuals have come in for a DoD in-person screening visit. *See below table.*
Screen individuals for participation in study	Ongoing. We have completed screening (includes first in-person screening visit and medical clearance) for 11 participants. *See below table.*
Enroll participants and study completion	Participant enrollment is ongoing. Five participants have completed study procedures. One participant dropped out of the study for personal reasons (receiving employment). One participant was excluded from the study due to delayed sedation. One participant was no longer eligible for the study by the baseline visit as he no longer met inclusion/exclusion criteria. One patient did not show up for her baseline appointment and cannot resume study procedures until January. Two patients have been medically cleared and are scheduled for infusions in January. *See below table.*

Phonescreens	108
In-person screens	22
Enrolled	11
Randomized	7
Completed infusion 1	7
Completed infusion 2	5
Completed study	5
Early withdrawal	2
Serious adverse event	0

To date, 108 phone screens were conducted for the DoD study since the end of March. Of these phone screens, 57/108 individuals were excluded over the phone as they did not meet inclusion/exclusion criteria. For example, some individuals suffered a loss of consciousness, could not be taken off their medication or suffered from a serious,

unstable medical illness. Since 2/17/09, 51/108 individuals were scheduled for an in-person screening appointment of which 29/51 did not come to the clinic. All 22/51 individuals that came to the clinic signed the Mood and Anxiety (MAP) consent form. Of these 22 individuals, 8 were lost to follow-up and 3 were excluded for not meeting the inclusion/exclusion criteria. Eleven of these 22 individuals showed up for their medical clearance, the second screening appointment, and signed the Department of Defense (DoD) consent form for the present study. All individuals were scheduled for an infusion. One of the 11 individuals scheduled for an infusion was lost to follow-up after signing the DoD consent form. This individual called the research coordinator two weeks later to explain the circumstances and would like to participate in the study later on in the year. Another individual was screened during the month of August, went on vacation, and returned in November at which point he no longer met the inclusion criteria of a minimum of 50 on the CAPS the day before the infusion. Two individuals are scheduled for infusions in January. The remaining 7 individuals who signed the DoD consent form received their first infusion. One individual dropped out of the study before the second infusion after receiving employment. Another individual was exited out of the study after the first infusion, in the middle of the first follow-up phase, due to delayed sedation 36 hours post-infusion. The remaining five patients completed all study procedures.

Key Research Accomplishments

- See above for recruitment details
- The present study is ongoing and will not be unblinded for interim review.

Reportable Outcomes

- Abstract for poster presented by Dr Adriana Feder at the annual Military Health Research Forum in Kansas City, MO, September 2009.

KETAMINE AS A RAPID TREATMENT IN POST-TRAUMATIC STRESS DISORDER
Marije aan het Rot, Ph.D., Adriana Feder, M.D., Dennis S. Charney, M.D., Sanjay J. Mathew, M.D., David L. Reich, M.D.

Conclusion

The present study is ongoing and will not be unblinded for interim statistical analysis.

References

The present study is ongoing and will not be unblinded for interim statistical analysis.

Appendices

See attached abstract and poster.

Supporting Data

The present study is ongoing and will not be unblinded for interim statistical analysis.